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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE: BATES, James N.	**APPEAL NO. _____**
SERIAL NO: 09/879,710	
FOR: S-METHYLCYSTEINE, S-ETHYLCYSTEINE, AND RELATED S-ALKYLTHIOLS AS ANTAGONISTS TO THE EFFECTS OF S-NITROSOTHIOLS AND NITRIC OXIDE	
	BRIEF ON APPEAL
FILED: June 12, 2001	
GROUP ART UNIT: 1651	

To the Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sirs:

Please enter the following Brief on Appeal into the record.

I. INTRODUCTION

This is an appeal of the Final Rejection dated April 23, 2002, finally rejecting claims 1-8. The appealed claims 1-8 are set forth in an attached Appendix.

II. REAL PARTY OF INTEREST

The real party of interest in the present appeal is University of Iowa Research Foundation.

III. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

IV. STATUS OF CLAIMS

Claims 1-8 were originally submitted June 12, 2001. In response to an Office Action dated September 13, 2001, Appellant amended claims 1, 7, and 8 and canceled claims 9-11. Subsequently, in a response to a Final Office Action dated April 23, 2002, Appellants amended claims 7 and 8; however, these amendments were not entered as raising new issues.

The claims here appealed are claims 1-8 as they appear after the timely response to the first office action, sent in on December 13, 2001.

V. STATUS OF AMENDMENTS

A Notice of Appeal was timely filed on August 16, 2002.

VI. SUMMARY OF INVENTION

The present invention is directed to therapeutic methods involving the administration of antagonist of S-nitrosothiols. S-nitrosothiols are naturally occurring compounds related to nitric oxide which are involved in the regulation of blood pressure, pain perception, control of smooth muscle tone, and numerous other functions in humans. (Specification (Spec.) p. 1, lines 5-10).

Preferred compounds of the present invention can generally be described as S-alkylthiols. (Spec. p. 3, lines 23-24). Most preferred are those that are S-alkylthiols of certain amino acids. (Spec. p. 3, lines 24-25). Particularly preferred are S-ethyl-L-cysteine,

S-methyl-L-cysteine, S-ethylglutathione, S-methylglutathione, S-methylcysteamine, S-ethylcysteamine, S-methylcoenzyme A, and S-ethylcoenzyme A. (Spec. p. 3, lines 26-29).

The treatment of patients may be with the compound of the present invention or their salts. (Spec. p. 3, lines 30-31). Such salts include salts with pharmacologically acceptable cations including, e.g., alkaline or alkaline-earth metals, specifically sodium, potassium or calcium, or salts with physiologically acceptable bases, e.g., simple amines such as ammonia. (Spec. p. 3, line 31 to p. 4, lines 1-4). Also included are salts with pharmacologically acceptable anions including, e.g., chloride, bromide, iodide, sulfate, and phosphate.

Liposomes may also be employed as carriers, wherein the compounds of t he present invention are present in the lumen of the liposome. (Spec. p. 4, lines 24-26). Preparation of liposomes is conventional and is extensively described in the literature, and need not be describe here. (Spec. p. 4, lines 26-28). A further improvement in delivery of the therapeutic agent can be achieved, for those diseases where the disease is associated with specific cells, by conjugating the liposomes molecules which provide for specific targeting. (Spec. p. 4, lines 28-32).

Any convenient mode of administration of the compounds of the present invention may be employed. (Spec. p. 5, lines 1-2). Administration may be oral, parenteral, via an enema, topical, or the like, such as by injection, oral tablet or powder solutions or other convenient means. (Spec. p. 5, lines 2-5).

The compounds of the present invention are administered in an amount sufficient to treat the disease. (Spec. p. 5, lines 8-9). An amount adequate to accomplish this is defined as

a "therapeutically effective amount" or "efficacious amount". (Spec. p. 5, lines 8-11). Amounts effective for this use will depend upon the severity of the condition, the general state of the patient, the rout of administration, and other factors known to those skilled in the art. (Spec. p. 5, lines 11-15). The specification provides dosage levels of from 100 mg to 10 g. (Spec. p. 5, line 15-17).

VII. ISSUES

The issues on appeal are:

A. Whether claim 8 contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

B. Whether claims 1-8 are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as his invention because the Examiner argues the phrase "consisting essentially of" is vague and indefinite since it is unclear from the specification as to what "consisting essentially of" would exclude;

C. Whether claims 1, 2, 7, and 8 are anticipated by Meisner et al. (U.S. Pat. No. 4,772,591) under the theory of inherency pursuant to 35 U.S.C. § 102(b); and

D. Whether claims 3-6 are unpatentable over Meisner under 35 U.S.C. § 103(a).

VIII. GROUPING OF THE CLAIMS

Claims 2-8 rise or fall with claim 1 on prior art issues.

Claim 1 sets forth: a method of counteracting the overproduction of nitric oxide which often occurs in hypotension and shock consisting essentially of administering to a patient a therapeutically effective amount of an S-alkylthiol as an antagonist of S-nitrosothiols.

IX. ARGUMENT

A. Claim 8 is an Obvious Typographical Error, However Applicants Amendment was Not Entered Into the Record

Claim 8 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner acknowledges that Applicants intended to claim 100 mg to 10 g, which is supported by the specification. Applicants traverse this rejection.

applicant also wanted to enter in "intravenously" which takes new issues

Applicants respectfully submit that claim 8 is a typographical error. The specification at page 5 clearly states 100 mg. However, Applicants Amendment After Final which corrected this error was refused entry into the record. This rejection should be reversed and the amendment entered as fully supported and not raising new issues.

B. Claims 1-8 Are Not Indefinite Based In The Usage Of The Term "Consisting Essentially Of" Under 35 U.S.C. 112, Second Paragraph

Claims 1-8 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. The Examiner argues that the phrase "consisting essentially of" is vague and indefinite since it is unclear from the specification as to what "consisting essentially of" would exclude. Appellants respectfully traverse this rejection.

See MPEP 2111.03

1. The Partially-Closed Language of Claim 1 Precludes the Addition of Ingredients That Would Destroy the Effects of S-alkylthiols as an Antagonist to S-nitrosothiols in Appellants' Claimed Method

The preamble of claim 1 includes the well understood partially closed transition phrase "consisting essentially of" which precludes "additional unspecified ingredients which would affect the basic and novel characteristics of the product [method] defined in the balance of the claim. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1574 (Fed. Cir. 1984). This language therefore excludes the addition of ingredients that would destroy the effects of S-alkylthiol as an antagonist to S-nitrosothiols since this would destroy the basic and novel characteristics of Appellants' claimed invention.

As stated by the MPEP, the phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. (MPEP § 2111.03). Such characteristics, i.e., operability to counteract the overproduction of nitric oxide, is therefore a measuring limit with respect to the prior art and its relevancy.

There is no indefiniteness in using "consisting essentially of" as the transitional phrase of a claim. Its meaning has been judicially interpreted and accepted for perhaps 100 years! The rejection should therefore be reversed.

C. Claims 1, 2, 7, and 8 are Not Anticipated by Meisner et al. Under 35 U.S.C. § 102(b)

Claims 1, 2, 7, and 8 were rejected under 35 U.S.C. § 102(b) as being anticipated by Meisner et al. (U.S. Pat. No. 4,772,591) for reasons of record which follow. The Examiner argues that Meisner teaches that a composition containing among other ingredients, an anti-inflammatory substance, specifically, S-methylcysteine, is administered to a patient. (See U.S. Patent No. 4,772,591 Abstract, col. 5, lines 3-27; col. 6, lines 6-8, 57-67; and the claims). The Examiner argues even though the composition is administered to the patient for a different reason in the reference, it would have been inherent to the process of Meisner that nitric oxide synthesis is inhibited since the steps of the processes (Meisner and the instant application) are the same. All the process requires is that the S-methylcysteine is administered to a patient, according to the Examiner.

Additionally, the Examiner argues that Applicants previous argument with respect to added ingredients in Meisner is moot because while Applicants argued that Meisner has other components in it besides the S-methylcysteine such as calcium, ascorbic acid, etc., the Examiner noted on page 4 of the instant specification that applicants also contemplate including calcium, antioxidants (of which ascorbic acid is commonly used) and the like in with their composition of S-methylcysteine as well.

Also, the Examiner states that Applicants previously argued that the composition of Meisner was administered in a different way. Meisner teaches administration of the composition in a variety of way including oral and topical. The Examiner concludes that

since these ways of Meisner include parenteral, the argument is moot. Appellants respectfully traverse this rejection.

1. Anticipation by Inherency

"Under the doctrine of inherency, if an element is not expressly disclosed in a prior art reference, the reference will still be deemed to anticipate a subsequent claim if the missing element "is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Id. at 1269, 20 U.S.P.Q.2d at 1749 (quoting In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981). The general rule is that inherency may be relied upon where and only where the consequence of following the reference disclosure always inherently produces or results in the claimed invention. See, e.g., W.L. gore Associates Inc. v. Garlock Inc., 220 U.S.P.Q. 303, 314 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). If there is not a reasonable certainty that the claimed subject matter will necessarily result, the rejection fails. See In re Brink, 164 U.S.P.Q. 247 (C.C.P.A. 1970).

For a claim to be inherent it "is not sufficient that a person following the disclosure sometimes obtain the result set forth in the [claim]; it must invariably, i.e., always happens. Standard Oil Co. (Indiana) v. Montedison, S.p.A., 664 F.2d 356, 372, 212 U.S.P.Q. 324, 341 (3d Cir. 1981). Likewise, "[i]n relying upon the theory of inherency, the examiner must

provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." Ex parte Levy 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Int. 1990).

2. Nitric Oxide Inhibition Does Not Necessarily Flow From The Method of Meisner

For inherency to attach, Meisner's administration of S-methylcysteine must be shown to invariably, always inhibit the effects of nitric oxide synthesis and be added in an amount sufficient to accomplish the inhibition. Although Meisner contemplates using as an anti-inflammatory, an amino acid such as S-methylcysteine, her final composition is not characterized as inhibiting nitric oxide synthesis, and it contains other things that would materially alter the compositions performance, i.e., a stimulant of epinephrine or nor-epinephrine production selected from tyrosine and phenylalanine and a anti-inflammatory. In the Meisner reference, methionine and cysteine can substitute for S-methylcysteine and are even preferred by Meisner. (Patent '591, col. 4, lines 56-58). Meisner also prefers glucosamine, other amino acids, and other non-sulfur-containing amino acids. (Patent '591, col. 3, line 64; col. 4, line 52). Conversely, in the present application, the sulfur side chains of the amino acid is essential, as is the S-methyl or S-ethyl group. Therefore, adding a composition with non-sulfur containing amino acids, as preferred by Meisner along with her other required added ingredients would materially affect the basic and novel characteristics of the claimed invention, i.e., S-methylcysteine as an antagonist to S-nitrosothiols. Additionally, Meisner administers tyrosine, which if taken intravenously, particularly at high

doses has been shown to produce a hypotensive response in a rat model. (See Ekholm, S. & Karppanen, H. (1987). Cardiovascular effects of L-tyrosine in normotensive and hypertensive rats. Eur J. Pharmacol, 143(1), 27-34). Thus, the administration of tyrosine at high doses would materially affect the novel characteristics of an embodiment of the present invention, which is to counteract the effects of hypotension. (See Spec. p. 2, line 17-19). Therefore, the phrase "consisting essentially of" does not render claims 1-8 vague and indefinite, but distinguishes the art. Applicants respectfully request this rejection be reversed.

Furthermore, Meisner's method of using her composition is incapable of inhibiting nitric oxide synthesis. Meisner's patent is for topical or oral applications. (Patent '591, col. 6, lines 14-20; col. 6, lines 39-40). The administration of S-methylcysteine, which is only included as an alternative amino acid and not a preferred one (Patent '591, col. 5, lines 3-27), will not likely produce any clinical effects because S-methylcysteine is a polar compound. It is well known in the art that polar compounds are absorbed poorly through the skin and whatever absorption that may occur would be so slow that significant serum levels would not be achieved. Furthermore, oral ingestion of S-methylcysteine in humans has shown no hemodynamic effects, therefore, no affect on blood pressure. Therefore, there is not a reasonable certainty that the topical application and oral ingestion of S-methylcysteine pursuant to Meisner's method causes nitric oxide inhibition. Moreover, parenteral does not include oral and topical administration as asserted by the Examiner. Parenteral, according to Stedman's Medical Dictionary, is defined in part as "referring particularly to the introduction of substances into an organism by intravenous, subcutaneous, intramuscular, or

intramedullary injection." On the contrary topical, is defined as "relating to a definite place or locality; local." In addition, oral is defined as "relating to the mouth. " (See Stedman's Medical Dictionary, 26th ed. (1995). Therefore, parenteral, does not include oral and topical administration.

Additionally, the Examiner has provided no basis in fact and/or technical reasoning to reasonably support the determination that Meisner's administration of S-methylcysteine inherently or necessarily would inhibit nitric oxide synthesis. Meisner does not provide any prophetic or working examples revealing the process conditions employed to produce such an effect. Therefore, there is no cogent technical reasoning and/or conclusive evidence to support the conclusion of the Examiner.

3. Conclusion as to Anticipation

For all of the above-stated reasons, Meisner et al. does not inherently anticipate claims 1-8 under 35 U.S.C. § 102(b). Appellants therefore respectfully request that the Examiner's rejection in this regard be reversed.

D. Claims 3-6 are Not Rendered Obvious by Meisner et al. Under 35 U.S.C. § 103(a)

Claims 3-6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Meisner (U.S. Pat. No. 4,772,591) for the following reasons of record, which include those under §102(b).

The Examiner argues that Meisner teaches that a composition containing "among other ingredients" (emphasis added), an anti-inflammatory substance, specifically, S-

methylcysteine is administered to a patient. (See abstract, col. 5, lines 3-27; col. 6, lines 6-8 and 57-67, and the claims of U.S. Patent No. 4, 772,591). The Examiner argues even though the composition is administered to the patient for a different reason in the reference, it would have been inherent to the process of Meisner that nitric oxide synthesis is inhibited since the steps of the processes (Meisner and the instant application) are the same. All the process requires is that the S-methylcysteine is administered to a patient.

The Examiner further states it is not clear from the reference if the S-methylcysteine is an S-methyl-L-cysteine form and it is not clear if the S-methylcysteine is a pharmaceutically acceptable salt form. If the composition does contain S-methyl-L-cysteine or is not in a pharmaceutically acceptable salt form, then it would have been obvious to use either of these since L forms of amino acids are well known to exist in the body and pharmaceutically acceptable salt forms of amino acids are well known in the art since such salts are routinely used and pharmaceutical preparations to improve solubility, for example. Thus, the Examiner argues, the claimed subject matter is anticipated by the reference or in the alternative, obvious over the cited reference. Applicants respectfully traverse this rejection.

1. Anticipation by Inherency

When anticipation is based on inherency of limitations not expressly disclosed in the assertedly anticipating reference, it must be shown that the undisclosed information was known to be present in the subject matter of the reference. Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1269, 20 U.S.P.Q.2d 1746, 1749-50 (Fed. Cir. 1991). An inherent limitation is one that is necessarily present; invalidation based on inherency is not

established by "probabilities or possibilities." Scaltech, Inc. v. Retec/Tetra, LLC., 178 F.3d 1378, 1384, 51 U.S.P.Q.2d 1055, 1059 (Fed. Cir. 1999).

2. Nitric Oxide Inhibition Is Not Inherent to the Process of Meisner Just Because All the Process Requires Is The Administered Of S-methylcysteine

The Examiner asserts all the process requires is that the S-methylcysteine is administered to a patient, but it cannot be administered along with other things that materially affect the ability to inhibit nitric oxide formation. In this Meisner fails because, as stated previously, Meisner prefers glucosamine, other amino acids, and other non-sulfur-containing amino acids (Patent '591, col, 4 lines 56-58). In the present application, the sulfur side chains of the amino acid is essential too, as is the S-methyl or S-ethyl group. Additionally, Meisner administers tyrosine, which if taken intravenously, particularly at high doses, has been shown to produce a hypotensive response in a rat model. Therefore, the process of nitric oxide synthesis inhibition in Meisner is not inherent. Applicants respectfully request for this rejection to be reversed.

3. The Law of Obviousness

The PTO bears the burden of establishing a case of prima facie obviousness. In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988). The critical inquiry for obviousness is whether "there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1558 (Fed. Cir. 1985). In other words, obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some

teaching or suggestion supporting the combination." In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988), quoting ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577 (Fed. Cir. 1984). This suggestion cannot stem from the applicant's own disclosure, however. In re Ehrreich, 590 F.2d 902 (CCPA 1979).

4. The Examiner Has Applied The Incorrect Standard Under §103 to Prove Obviousness of Using A Pharmaceutically Acceptable Salt Form of S-methylcysteine

Obvious-to-try is not the test for patentability under 35 U.S.C. § 103. See In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988). The Examiner has used the incorrect standard for obviousness. By asserting that "if the composition does not contain S-methyl-L-cysteine or is not in pharmaceutically acceptable salt form, then it would have been obvious to use either of these since L forms of amino acids are well known to exist in the body and pharmaceutically acceptable salt forms of amino acids are well known in the art since such salts are routinely used in pharmaceutically preparations to improve solubility, for example." As acknowledged by the Examiner Meisner's disclosure itself does not contain a sufficient teaching of this matter. Therefore, the Examiner has used an incorrect standard of obviousness and has failed to establish a prima facie case. Applicants respectfully request for this rejection to be reversed.

5. Meisner Fails to Appreciate Appellants' Claimed Method of Administration of An Antagonist to S-nitrosothiols To Reduce The Risk of Conditions Such As Hypotension

Where the reference does not appreciate the existence of the problem solved by the invention, the applicant's recognition of the problem is, in itself, strong evidence of the non-

obviousness of the invention. In re Nomiya, 184 USPQ 607, 612-13 (CCPA 1975). Meisner teaches that "the wound healing process can be favorably affected by administration of a composition comprising a mild anti-inflammatory agent and substances which in combination have been found to accelerate fibrous tissue growth." (See col. 2, lines 49-55). Conversely, Applicants embodiment focuses on a therapeutic method that specifically counteracts the hypotension caused by the overproduction of nitric oxide and nitrosothiols as present in conditions such as septic shock. (Spec. p. 2, lines 17-24). The recognition of the source of this problem is what is unobvious and Meisner fails to contemplate or disclose such a problem. There is no effective treatment presently available that specifically-counteracts the hypotension caused by the relative overproduction of nitric oxide and nitrosothiols as present in such conditions as septic shock. (Spec. p. 2, lines 19-23). Current treatment options for hypotension or shock from such conditions such as septic shock, toxic shock syndrome, spinal cord injury, effects of anesthetics, and anaphylaxis, etc. are limited to vasoconstricting agents that have many deleterious side effects that therefore limit their effective therapeutic usage. (Spec. p. 2, lines 11-16). On the contrary, Meisner's method is directed at treatment of wound healing and use of S-methylcysteine is not pertinent to the problem being solved. Applicants respectfully request this rejection be reversed.

6. There is No Suggestion or Motivation to Modify the Teachings of Meisner to Obtain the Claimed Invention

The Federal Circuit stated in In re Fritch that the "examiner can satisfy burden of obviousness in light of combination 'only by some objective teaching [leading to the

combination]'" In re Fritch, 972 F.2d 1260, 1265, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). A parallel test applies when an obviousness rejection is based on a single reference. "When obviousness is based on a particular prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference." B.F. Goodrich Co. v. Aircraft Braking Sys. Corp., 72 F.3d 1577, 1582 (Fed. Cir. 1996).

There is no showing of a suggestion or motivation to modify the teachings of Meisner to use S-methylcysteine in a pharmaceutically acceptable salt form. The Examiner states in the Office Action dated September 13, 2001, that "[i]t is not clear from the reference if the S-methylcysteine is in S-methyl-L-cysteine form and it is not clear if the S-methylcysteine is in a pharmaceutically acceptable salt form." (Office Action p. 6, lines 8-10). Therefore, the Examiner has not satisfied a prima facie case of obviousness because he has failed to show some objective teaching to modify the teachings of Meisner. Appellants respectfully request for this rejection to be reversed.

7. Conclusion as to Obviousness

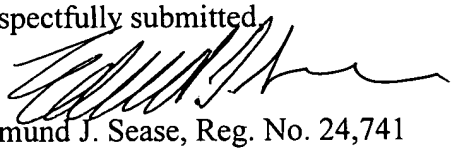
For all of the above-stated reasons, the claimed invention is not rendered anticipated or in the alternative obvious over Meisner et al. The Examiner's rejection in this respect should therefore be reversed.

X. CONCLUSION

For the above-stated reasons, it is respectfully submitted that the claims are in a condition for allowability. The decision of the Examiner, therefore, should be reversed and the case allowed.

Enclosed herein please find the appeal brief in triplicate and required fee of $160. If this amount is not correct, please consider this a request to debit or credit Deposit Account No. 22885 accordingly.

Respectfully submitted,



Edmund J. Sease, Reg. No. 24,741
McKEE, VOORHEES & SEASE
Attorneys of Record

801 Grand - Suite 3200
Des Moines, Iowa 50309-2721
515-288-3667 - tb -

APPENDIX

1.

A method of counteracting the overproduction of nitric oxide which often occurs in hypotension and shock consisting essentially of:

administering to a patient a therapeutically effective amount of an S-alkylthiol as an antagonist of S-nitrosothiols.

2.

The method of claim 1 wherein the S-alkylthiol is selected from the group consisting of S-ethylcysteine, S-methylcysteine, S-methylcysteamine, S-ethylcysteamine, S-ethylglutathione, S-methylglutathione, S-methylcoenzyme A, and S-ethylcoenzyme.

3.

The method of claim 1 wherein the S-alkylthiol is selected from the group consisting of S-ethyl-L-cysteine, S-methyl-L-cysteine, S-ethylglutathione, S-methylglutathione, S-methylcysteamine, S-ethylcysteamine, S-methylcoenzyme A and S-ethylcoenzyme A.

4.

The method of claim 1 wherein the S-alkylthiol is a pharmaceutically acceptable salt form.

5.

The method of claim 2 wherein the S-alkylthiol is a pharmaceutically effective salt form.

6.

The method of claim 3 wherein the S-alkylthiol is a pharmaceutically acceptable salt form.

7.

The method of claim 1 wherein administration is parenterally.

8.

The method of claim 1 wherein the dose ranges from about 1 mg* to about 10 grams.

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* This is a typographical error. The specification at page 5, line 16 clearly says 100 mg. However, Applicants Amendment After Final, which corrected this, was refused entry.

CERTIFICATE OF MAILING

I hereby declare that the attached Patent Application and filing fee has been mailed by U.S. Postal Service's "Post Office to Addressee" Express Mail service in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C., 20231, prior to 5:00 p.m. on the 15th day of October, 2002.

Ruth A. Lourens

Ruth A. Lourens
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